With author's compts.

LEUKOSIN.

A NEW SUBSTANCE FOUND IN THE BLOOD OF LEUKAMIA.

also B. M. S. Journal, Nov. 28. 1878.

ALSO A DESCRIPTION OF ANOTHER CRYSTALLINE BODY FOUND IN THE VOMITUS.

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[Read before the Boston Society for Medical Observation, and communicated for the Boston Medical and Surgical Journal.]

DURING the present winter two cases of leukämia, or leucocythemia, have been observed in this city. One of these has been fully reported to a meeting of the Medical Improvement Society by Dr. H. J. Bigelow. The second occurred at the Massachusetts General Hospital, under the care of Dr. H. I. Bowditch, and will be noticed by him at a future meeting of the same Society. Dr. Ellis made the *post-mortem* examination in this latter case, and gave me the blood to analyze. Leaving to him, therefore, the complete description of its pathological condition, which corresponds exactly to that usually met with in this disease, I shall confine my remarks merely to the chemical changes noticed in this and similar instances.

As long ago as 1845, Rudolph Virchow examined a body and found the liver, spleen and lymphatic glands enlarged, and at the same time the blood changed in a manner, being composed, in fact, to a large extent, of the colorless corpuscles. With that admirable sagacity peculiar to the man, he saw at once that this was something very different from those cases described as pyamia by previous observers, and, to distinguish it, called the disease leukämia. During the next four years he discovered three other cases, which he published from time to time, and in which he insisted upon this unnoticed connection between the enlargement of the blood-glands and the characteristic excess of white corpuscles in the blood, urging the German physicians to increased attention to this disease. It was likewise in 1845 that Bennett observed and described "a case of hypertrophy of the spleen and liver, in which death took place from suppuration of the blood." Of the real nature of this case, however, he was so profoundly unsuspicious that he even labored

to deny the true theory of the disease, and said, "with regard to the colorless corpuscles of the blood, we know of no instance where they existed in the amount, or presented the appearance described." It was not till six years afterward, during which time Virchow had been deeply engaged in observing and publishing facts which corroborated his original opinion, and not until his views had been generally recognized and adopted, throughout Germany at least, that Bennett appears in public, and describes this same disease, in an analysis of cases, under the name leucocythemia. He would have us give up the original name of leukämia, or "white blood," which should always remain associated with the labors of the great discoverer of the disease, because, he says, the blood, when drawn from the arm, is not white, and adopt the name leucocythemia, or white-cell blood.

Now Virchow objects to any such change, because the blood, after death, is really marked by white patches, and Bennett's name is equally a misnomer, inasmuch as cases occur where no white cells are found, and only nuclei or naked kernels are present. The objection can also be raised against it that all normal blood is white-cell blood. The name leukämia was in fact first given in order to prove that blood may have a yellowish-white appearance, like pus, without being pus. When, then, all the credit of the discovery of this disease is given to Bennett, we cannot wonder that Virchow writes as follows: "It is very strange that there is still any question as to priority. When one has been obliged for more than four years, without support, and almost without recognition, both to write and to speak over and over again for the introduction of a new truth in pathology; when one has been obliged from the very first to deny the suppurative character of this change in the blood, in opposition to the views of well-known observers, and especially Bennett, it might seem that the matter was clear enough." With the Dublin *Medical Press*, he wonders, then, at "this free and easy appropriation of other men's intellectual products." Let us, then, not rob this greatest of modern pathologists, to whom we owe so much, of the smallest mite of merit so justly due him.

The chemical analysis of the blood is, under the most favorable and normal conditions, a difficult and unsatisfactory matter; for authorities still differ as to what is serum and what plasma, and different chemists give us quite different results. It is with much circumspection, then, that we should receive the quantitative analysis quoted by Bennett in his monograph on this disease; for very little blood could be drawn from the patients while living, and after death the relative proportions of the fluid and solid properties change rapidly. Moreover, but few examinations have been made, too few for us to draw from them any just conclusion. We may, however, safely infer from the light specific gravity uniformly observed (ranging from 1036 to 1049, while the average of nor-

mal blood is 1055), that the volume of *water* is increased, and the solid matter diminished. This at first sight seems hardly probable, when we remember the enormous amount of coagula found distending the heart and vessels after death, but at the same time it proves that the colorless corpuscles must contain a relatively trifling amount of solid matter. With the decrease of the red corpuscles the *iron* is also found to be proportionally diminished. According to the analysis quoted by Bennett, the *fibrine* in this disease is considerably increased; but more reliable investigations show that this substance, as well as the *albumen* and the *salts* of the serum, remain in their relatively normal proportion.

By far the best analysis yet made of the blood in leukämia is that of Scherer, who had previously discovered the presence of hypozanthin in the spleen. He obtained the following results from the examination of the blood of a subject dissected by Virchow himself.

Quantitative.

Water,	791.7				
Solid matter,	208.3	Organic constituents,	197.300		
		Inorganic "	11.084	Iron,	0.298
				Earthy phosphates,	0.598

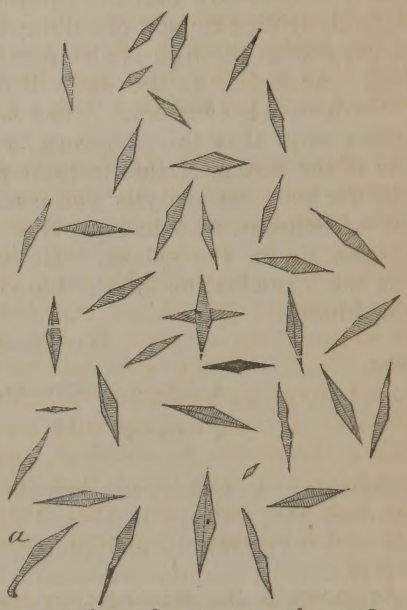
Submitting it to a thorough investigation, he made the interesting discovery that formic, lactic and acetic acids were present, together with hypozanthin and gluten. Hypozanthin is a substance closely allied to zanthic oxyd and uric acid, and its presence in the blood in connection with the frequent urinary deposit of the latter in this disease is well worthy of note, and may prove a valuable diagnostic sign. It is with reference to these important discoveries of Scherer that I have brought this subject before the Society, in order to make known the presence of another new principle in the blood of leukämia.

The specimen given me for examination was a dirty reddish-brown color, and had a conserve-like density, the upper parts of the coagula being in spots marked by white concretions of the colorless corpuscles. It was very slightly acid, and had a fishy odor, although no decomposition had taken place. On microscopic examination, in addition to the usual appearance of red and colorless corpuscles, &c., numerous minute crystals were noticed, such as I had never seen before. In the blood removed from the cavities of the heart, the large vessels, and from the spleen, they were very abundant, while the portal circulation contained fewer. In a large exudation, or abscess, situated in the cellular tissue beneath the left axilla, none were observed, although in other respects its microscopic characteristics closely resembled those of the blood. The crystals, unfortunately, are of the same specific weight as the white corpuscles, and therefore cannot be isolated for a separate analysis.

They are colorless, transparent, and appear to be faintly-mark-

ed, elongated, rhombic octahedra, with sharp outlines in profile. In a few instances they are united by pairs, the long axes crossing each other at right angles. Many of them differ from the true type of crystallization, being extremely elongated, and exhibiting incurved faces and such irregularities of form, as to prove their organic nature. (Fig. 1.) This supposition is entirely confirmed by the result of incineration, to which on being submitted no residue was left. In sulphuric and hydrochloric acids they are quickly dissolved. In a solution of caustic potash they are readily soluble, but no ropiness is produced by its addition to the blood, as would be the case if pus were present. In acetic acid they are also soluble, though slowly. In concentrated nitric acid they are, strange to say, completely insoluble, even when heated, and assume a faint yellow hue. By its action their acute angles are sometimes bent upon themselves, as seen in Fig. 1, *a*. In cold and hot water they are alike insoluble, and they remain unaffected by alcohol, ether, benzole and ammonia. Judging by their behavior in the presence of the above re-agents, it is plain they are the crystals of a substance which must range itself in the class of neutral principles, and as nothing similar has ever been found either in healthy or abnormal blood, or in any part of the animal economy, so far as the latest chemical reports show, I propose for it the name of leukosin. This title seems appropriate, both on account of the color of the crystals and the disease in which they were discovered.

Fig. 1.

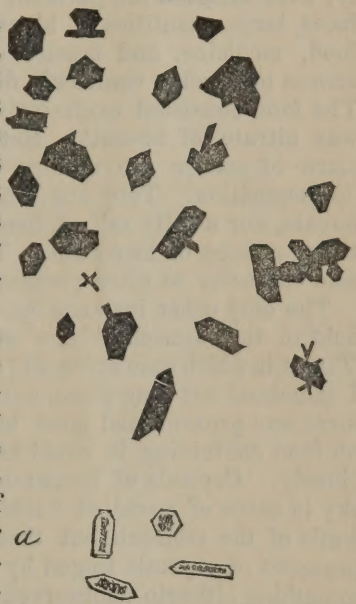


The blood of leukämia is very like the natural condition of this fluid in the splenic system. Scherer first discovered in the spleen the very substances which he afterward demonstrated in this disease, and the crystals often found in this organ, lozenge shapes of a reddish-yellow color, and described by many observers, Becquerel tells us were present in great abundance in the coagula removed from the heart in a case of leukämia. That the spleen is not the sole cause of the changes in the blood, is shown by the facts, that this organ is often otherwise affected without any consequent similar change, and that in some cases of leukämia it is found in a normal condition. The other blood or lymph glands, on the con-

trary, are always found diseased. At all events, the presence of so much abnormal matter in the blood, penetrating every atom of the human frame, must be sufficiently deleterious to account for the peculiar symptoms of the disease, though it is evident that in the present state of our knowledge we are far from being able to solve its mysterious etiology; but whether the state of the blood be the prime cause of it, or merely its result, all observations which tend to throw light upon its chemical composition must be received as important facts bearing upon its future solution.

In connection with the above case, I would describe here other crystals discovered in the vomitus of a patient of Dr. Gould, in whom hæmatemesis was present as a symptom of cancer of the stomach. The amount of the hæmorrhage was considerable; and on examination of the matter rejected, the crystals to be seen in Fig. 2 were found. They were at first looked upon as hæmatine, as this substance is not unfrequently met with in hæmorrhagic effusions, but on analysis it was found that this was not the case, and that they were some substance hitherto undescribed.

FIG. 2.



As shown in the drawing, they are sections of a hexagonal prism, some faces of which are irregularly elongated. By transmitted light they are of a reddish-brown color, while in reflected light they show a straw-yellow tinge. From the variety of form they assume, and their peculiar color, I presumed an organic composition, but, to my surprise, they retained their shape, sharply defined, even when submitted to a heat sufficient to melt glass. At a low temperature the coloring matter disappeared, without blackening or smoke. In nitric and hydrochloric acids they are slowly soluble, without effervescence. When placed in concentrated sulphuric acid, they retain for a long time their outline unchanged, but the coloring matter gradually disappears, leaving a granular appearance in their centre. (Fig. 2, *a*.) Potash also dissolves them, though slowly. By acetic acid and ether they are unaffected. From the effect of heat, as above applied, we see that we have here a difficultly fusible, inorganic base united with some unknown organic material, either mechanically or chemically. It would seem that the latter only plays the part of shadow, for after its entire decomposition by heat and acid, the

substance remains unchanged. Further analysis, as conducted by Dr. Bacon, showed that this matter was lime, but in what form it is impossible to ascertain. They may be crystals of some unknown salt of lime, into which the coloring matter of the blood has been taken up, just as frequently results when crystallization occurs in colored solutions of various sorts; or it may be the sole chemical compound of the base, a minute quantity only being sufficient to determine their formation, so little, in fact, that their shape and structure remain unchanged when it is driven off.

In so complex a mixture as is present in that laboratory, the stomach, it is difficult to say what compounds may not be formed, and especially so in a pathological case like the following. Here, in addition to the secretions from the healthy portions of the cavity, were mingled the purulent discharges from the ulcerating surfaces, large quantities of blood poured out from corroded vessels, food, medicine, and masses of penicilium and torula, and the spores of sarcina ventriculi, disposing the whole to fermentation. The food consisted exclusively of milk, and the only drug given was nitrate of bismuth. But the crystals separating from this maze of matter are nothing we might expect to result from its decomposition. They are neither lactate, butyrate, oxalate, carbonate, nor a fatty salt of lime, nor do they at all correspond to the re-actions of hæmatine. The vomitus itself had that pungent acid character so often present in this disease.

The only other instance on record of crystals occurring in the fluid of the stomach, is one described by Neale in the *Medical Times*, in which case uric acid [?] was found. In some vomitus which I examined not long since, oxalate of lime in its usual octahedral form was present, and must have been formed in the stomach, for no food containing it could have been eaten for a long time previously. Crystals of hæmatoidin have been observed by Rokitansky in cases of so-called "infarct," or apoplectic deposits in the walls of the stomach, but their occurrence in its cavity, or the presence of crystals tinged by the coloring matter of the blood, is something hitherto unobserved.

February, 1859.